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Reduced Default Mode Connectivity in Adolescents With Conduct Disorder

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Objective: Conduct disorder (CD) is characterized by impulsive, aggressive, and antisocial behaviors that might be related to deficits in empathy and moral reasoning. The brain's default mode network (DMN) has been implicated in self-referential cognitive processes of this kind.

Method: This study examined connectivity between key nodes of the DMN in 29 adolescent boys with CD and 29 age- and sex-matched typically developing adolescent boys. The authors ensured that group differences in DMN connectivity were not explained by comorbidity with other disorders by systematically controlling for the effects of substance use disorders (SUDs), attention-deficit/hyperactivity disorder (ADHD) symptoms, psychopathic traits, and other common mental health problems.

Results: Only after adjusting for co-occurring ADHD symptoms, the group with CD showed hypoconnectivity

between core DMN regions compared with typically developing controls. ADHD symptoms were associated with DMN hyperconnectivity. There was no effect of psychopathic traits on DMN connectivity in the group with CD, and the key results were unchanged when controlling for SUDs and other common mental health problems.

Conclusion: Future research should directly investigate the possibility that the aberrant DMN connectivity observed in the present study contributes to CD-related deficits in empathy and moral reasoning and examine self-referential cognitive processes in CD more generally.

Key words: conduct disorder, ADHD, psychopathic traits, default mode network, functional connectivity

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Conduct disorder (CD) is defined as a repetitive and persistent pattern of antisocial behavior in which the rights of others or societal norms are violated.¹ Symptoms of CD include theft, vandalism, and violence toward other humans and animals. Neuroimaging studies of CD have implicated dysfunction in the fronto-amygdala and fronto-insula circuits as part of a disrupted ventromedial/orbitofrontal-limbic network.²⁻⁴ Several recent studies also have suggested that the brain's default mode network (DMN) could be implicated.⁵⁻⁷ The DMN is comprised of the anterior medial prefrontal cortex (aMPFC), posterior cingulate cortex (PCC), medial temporal lobe (MTL), lateral parietal cortex, and temporal-parietal junction.⁸⁻¹⁰ The DMN consists of different subsystems,^{8,10,11} namely the dorsal MPFC (dMPFC) subsystem, the MTL subsystem, and the aMPFC-PCC core system. These subsystems are believed to play a critical role in self-referential cognitive processing, including the construction of mental representations of the self and one's own and others' possible future actions, thoughts, and feelings.^{12,13} In particular, the dMPFC subsystem is involved in theory of mind and morality judgments.^{13,14} The MTL subsystem is involved in binding together disparate information to facilitate scene construction⁸ and the aMPFC-PCC core in attaching personal

significance to internally focused thoughts,⁸ forming the self-other distinctions linked to prosocial behavior,¹⁵ and possibly forming judgments of affective empathy.¹⁶ Thus, the DMN and its component subsystems represent plausible pathophysiological substrates for deficits in emotion perception,¹⁷ empathy,¹⁸ and moral reasoning¹⁹ that have been observed in individuals with CD.

Using independent components analysis, Dalwani *et al.*⁶ found that, compared with typically developing controls, adolescent boys with CD showed decreased connectivity between the superior, medial, and middle frontal gyrus, lingual gyrus, retrosplenial cortex, and lateral temporal cortex, reflecting generalized DMN dysregulation in CD. However, all participants with CD also had substance use disorders (SUDs), which have been associated with DMN abnormalities.²⁰⁻²² Furthermore, the study did not include a dedicated rest period, instead using a task with alternating periods of rest and stimulus processing. This is problematic because DMN connectivity is affected by such variations in task characteristics²³ and instructions.²⁴ Another recent small-scale study²⁵ reported DMN hypoconnectivity in adolescent boys with CD who were free of comorbid SUDs, also using independent components analysis methods but, in this case, more standard procedures for collecting resting-state functional magnetic resonance imaging (fMRI) data.

In the present study, this analysis of DMN dysregulation in CD is extended several ways. First, a more theoretically driven seed-based approach was adopted, which is better suited to investigating which DMN subsystems are impaired



Supplemental material cited in this article is available online.

by restricting the analysis just to those regions shown to be involved in mental scene construction, socio- and non-social-cognitive conceptualization, and self-referential thinking.¹¹ This takes advantage of the functionally dissociable nature of DMN subsystems and has the potential to provide a more straightforward interpretation of underlying cognitive impairments. Indeed, such an approach has been used to identify DMN subsystem-specific abnormalities in schizophrenia and major depression.²⁶⁻²⁸

Second, the impact of clinical heterogeneity and comorbidity on the relation between CD and DMN connectivity was systematically examined. In particular, the impact of SUD comorbidity on DMN connectivity in CD was examined, given that all participants with CD in the study by Dalwani *et al.*⁶ had comorbid SUDs, whereas none of the participants in the study by Zhou *et al.*²⁵ reported SUD comorbidity. Epidemiologic studies have shown a high degree of overlap between CD and SUDs,^{29,30} so this is an important clinical issue, and the authors believed it was critical to replicate these findings suggesting that CD is associated with DMN abnormalities, irrespective of SUD comorbidity. This study also examined whether DMN abnormalities were related to psychopathic traits in the present CD sample. Psychopathy is a personality disorder characterized by a callous lack of empathy and impulsive antisocial behavior. Although the term *psychopathy* is not applied to adolescents, high levels of psychopathic traits are nevertheless associated with an increased risk of violent offending in participants with CD,^{31,32} and CD with elevated psychopathic traits has been suggested to represent a more pervasive subtype of CD.³³ Some studies have reported decreased connectivity between brain regions overlapping with core DMN midline regions in psychopathic adults.^{34,35} Interestingly, even within the construct of psychopathy, there might be differential effects of the affective/interpersonal and antisocial factors of psychopathy, with the affective/interpersonal factor associated with decreased medial-lateral DMN connectivity and the antisocial factor associated with increased connectivity between prefrontal and parietal DMN components.³⁶ However, to date, no study has directly investigated the effects of psychopathic traits on DMN connectivity in participants with CD. Adolescence is a developmental period in which there are widespread changes in structural connectivity³⁷ that can have a bearing on the developmental course of antisocial behavior and psychopathy. This makes it pertinent to examine whether altered DMN connectivity in those with psychopathy is observed at an earlier stage in development. In addition, the association between DMN dysregulation and attention-deficit/hyperactivity disorder (ADHD) symptoms was examined. ADHD is a neurodevelopmental condition characterized by persistent and age-inappropriate levels of inattention, hyperactivity, and impulsivity.¹ This condition frequently co-occurs with CD and is present in 25% to 30% of boys with CD.³⁸ Even in those who do not meet formal diagnostic criteria for ADHD, there is considerable overlap in symptomatology, and symptom dimensions of impulsivity and hyperactivity

have been associated with the development of antisocial behavior in childhood.³⁹ Notably, ADHD is associated with abnormal DMN connectivity, hypothesized to reflect a disorganization of the network and an inability to appropriately regulate self-generated thought.^{40,41} Third, this study examined whether there were differences in DMN connectivity according to the age of onset of CD—that is, whether DMN connectivity was altered in childhood-onset and adolescence-onset subtypes of CD or just the former subtype. Like psychopathy, the age of onset of CD is believed to differentiate between subtypes of CD that differ in etiology and adult outcomes.^{1,42} Childhood-onset CD, which emerges before 10 years of age, has been linked to distinct cognitive⁴³ and neurophysiologic⁴⁴ profiles compared with adolescence-onset CD, possibly reflecting the fact that these subtypes have different etiologies⁴⁵ (although see Fairchild *et al.*⁴⁶ for a review challenging this idea).

In summary, the authors examined DMN connectivity in adolescents with CD using a more hypothesis-driven approach than has been used previously to investigate distinct subsystems of the DMN. To this end, the authors used a seed-based approach that measured connectivity between *a priori* regions of interest in limited components of the extended DMN that might be involved in deficits in empathy and moral decision making observed in young people with CD.¹¹ The authors predicted that adolescents with CD would display a generalized decrease in DMN connectivity that would be especially pronounced in the subgroup with elevated psychopathic traits. They also predicted that these effects would not be accounted for by other comorbid conditions and therefore would persist when controlling for the effects of SUDs, ADHD, and other common mental disorders.

METHOD

Participants

Seventy adolescent boys 13 to 18 years old were recruited from schools, colleges, pupil referral units, and Youth Offending Teams in the Hampshire area of the United Kingdom. Of this total sample, 6 were excluded due to gross neurologic abnormalities (gray or white matter abnormalities and cysts), 3 for excessive head movement, and 3 due to major depressive disorder and/or general anxiety disorder comorbidity. This meant that data from 58 participants (29 with CD and 29 controls) were available for analysis. Sixteen participants had childhood-onset CD (i.e., ≥ 1 CD symptom before 10 years of age) and 13 had adolescence-onset CD (i.e., symptoms only after 10 years¹). Seven participants with CD had comorbid ADHD but were otherwise free of all other common co-occurring disorders (with the exception of oppositional defiant disorder). Healthy control participants screened negative for current psychiatric disorders using the same diagnostic instrument (see below).

Diagnostic Assessment

The Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL⁴⁷) was used to assess CD and other common mental disorders (e.g., major depressive disorder, general anxiety disorder, oppositional defiant disorder, ADHD, obsessive-compulsive disorder, and posttraumatic

stress disorder). The K-SADS-PL is a semistructured interview based on *DSM-IV* criteria.⁴⁸ If a symptom is endorsed at threshold by the child or the parent, then it is considered present.⁴⁷ Participants were given a research diagnosis of CD if they (or their parents) endorsed at least 3 CD symptoms in the past 12 months. Control participants were screened using the same instrument and were free of all assessed disorders and past diagnoses of CD or oppositional defiant disorder. All participants also completed the self-report Youth Psychopathic traits Inventory (YPI⁴⁹) to assess psychopathic traits. The YPI measures psychopathy as a multicomponent construct encompassing a grandiose and manipulative interpersonal style (factor 1), a callous and unemotional affective style (factor 2), and impulsive and irresponsible behavior (factor 3). Substance use was assessed using the Problem Severity scale of the Personal Experience Screening Questionnaire.⁵⁰ In line with recommended scoring guidelines, participants younger than 16 years with scores higher than 30 or those aged at least 16 years old with scores higher than 35 were assessed as being at high risk for SUDs. Sixteen of the 58 participants (12 from the CD group, 4 from the control group) were excluded from the supplementary analyses testing for group differences in the subsample without SUDs. Handedness was measured using the Edinburgh Handedness Inventory.⁵¹

Procedure

Initial assessment and screening took place on a day before the MRI scan. During this time, informed consent was obtained from the participant or the primary caregiver if the participant was younger than 16 years. Additional exclusion criteria were a clinical diagnosis of a neurodevelopmental (e.g., Down syndrome) or pervasive developmental (i.e., autism spectrum disorder) disorder, an estimated IQ lower than 75 as assessed using the 2-subtest version of the Wechsler Abbreviated Intelligence Scale,⁵² and standard MRI exclusion criteria (cardiac pacemaker, metal in body, claustrophobia, etc.). Eligible participants were invited to take part in an MRI scan lasting 35 to 40 minutes on a separate day.

Image Acquisition. The fMRI data were acquired on a 1.5-T Siemens Avanto (Siemens AG, Erlangen, Germany) MRI scanner at Southampton General Hospital in the United Kingdom. A 12-channel head coil was used to detect and receive the magnetic resonance signal. T1-weighted (MP-RAGE) 3-dimensional datasets (voxel size $1.2 \times 1.2 \times 1.2$ mm, repetition time 2,400 ms, flip angle 8° , 160 slices) were acquired, with an acquisition time of 7 minutes 41 seconds. These were obtained for registration and to create white

matter and cerebrospinal fluid masks used to generate confound regressors. Resting-state fMRI data were acquired using a T2*-weighted gradient echo planar imaging sequence (repetition time 3,600 ms, 35 slices, voxel size $3.26 \times 3.26 \times 3.26$ mm, in an interleaved acquisition, flip angle 90° , 123 volumes). The resting-state scan lasted 6 minutes 10 seconds. During the scan, participants were asked to relax and fixate on a red crosshair presented against a white background (i.e., eyes-open acquisition). Participants underwent the structural scan before the resting-state scans.

Image Preprocessing. The FSL 5 software package (<http://fsl.fmrib.ox.ac.uk>) and the Connectivity Toolbox 13 (<http://www.nitrc.org/projects/conn>⁵³) were used for image preprocessing. The first 3 volumes of each functional time series were discarded to allow for magnetic saturation effects. Participants were excluded if the relative head displacement was greater than 3 mm in the *x*, *y*, or *z* coordinates or the maximum rotation encompassing yaw, pitch, and roll was greater than 2° . Preprocessing steps included identifying outlier time points that were included as confound regressors in the first-level general linear model (motion scrubbing); a rigid-body correction for head motion; nonlinear registration of functional data to a T1-weighted Montreal Neurological Institute template that was resampled to $4 \times 4 \times 4$ mm³; spatial smoothing (gaussian full width at half-maximum kernel of $6 \times 6 \times 6$ mm³); an anatomic component-based strategy⁵⁴ (aCompCore) that involved regression of subject-specific time series from 6 components estimated from white matter and cerebrospinal fluid masks using principal components analysis; bandpass filtering (0.008–0.09 Hz); and de-spiking using a hyperbolic tangent function to decrease the influence of outlier scans.

Regions of Interest. Eleven a priori regions of interest were selected from coordinates provided by Andrews-Hanna *et al.*¹¹ to study connectivity in all 3 subsystems of the DMN associated with different internally mediated cognitive processes (Table 1 presents the details and relevant coordinates). Andrews-Hanna *et al.* identified these seeds in a young adult sample. Although there is evidence that long-range connectivity within the DMN continues to develop well into adolescence, by adolescence these changes are limited to increases in functional connectivity between nodes, with all major DMN nodes fully formed in childhood.^{55,56} Therefore, the authors believed they were justified in using these seeds in an adolescent population. All seeds were 8-mm radius spheres created using FSL. Consistent with previous studies,^{11,27,28} only left lateralized and midline regions were investigated in this study to prevent biasing connectivity to mirrored regions of interest.

TABLE 1 Default Mode Network Regions of Interest and Their Respective Montreal Neurological Institute (MNI) Coordinates

Subsystem	Region	Abbreviation	MNI Coordinates		
			<i>x</i>	<i>y</i>	<i>z</i>
Posterior cingulate-anterior medial prefrontal cortex core	posterior cingulate cortex	PCC	−8	−56	26
Dorsomedial prefrontal cortex subsystem	anterior medial prefrontal cortex	aMPFC	−6	52	−2
	dorsomedial prefrontal cortex	dMPFC	0	52	26
	temporal parietal junction	TPJ	−54	−54	28
	lateral temporal cortex	LTC	−60	−24	−18
	temporal pole	TP	−50	14	−40
Medial temporal lobe subsystem	ventral medial prefrontal cortex	vMPFC	0	26	−18
	posterior inferior parietal lobule	pIPL	−44	−74	32
	retrosplenial cortex	Rsp	−14	−52	8
	parahippocampal cortex	PHC	−28	−40	−12
	hippocampal formation	HF	−22	−20	−26

Statistical Analysis

The specific time series were computed by averaging the temporally filtered residual time series for each voxel within each seed. For each seed, bivariate correlation matrices were calculated yielding group-level β values that were Fisher transformed. Group comparisons used analysis of covariance to compare all participants with CD with healthy controls in the first instance; in addition, the adolescence-onset and childhood-onset CD subgroups were compared with healthy controls and the adolescence-onset and childhood-onset CD subgroups were compared. The influence of psychopathic traits on DMN connectivity was investigated using a linear regression analysis on the summed total YPI scores and each of the 3 separate factors of psychopathy (i.e., interpersonal, affective, and behavioral). For all second-level contrasts, age, IQ, and ADHD symptoms were included as covariates of no interest. ADHD is a disruptive behavior disorder that frequently co-occurs with CD and is independently associated with atypical DMN connectivity.⁵⁷ It was also important to control for age and IQ, given that development of the DMN continues well into adolescence⁵⁶ and intelligence has been associated with connectivity strength.⁵⁸ Results are reported at a threshold of a p value less than .05 (2-tailed), with false discovery rate correction at the level of the entire analysis (i.e., controlling for each seed and each target seed simultaneously). Given the small sample, comparisons between childhood-onset and adolescence-onset subtypes of CD and healthy controls were performed at an uncorrected α level of a p value less than .01 (2-tailed).

Ethics Approval. This study was reviewed and approved by the University of Southampton Ethics Committee, the University Research Governance Office, the Hampshire County Council Research and Evaluation Unit, Southampton City Council Children's Services Research Governance Committee, and the University Hospital Southampton National Health Service Trust's Research and Development Office.

RESULTS

The groups were well matched in age and handedness. The CD group had lower IQ scores, more ADHD symptoms, and higher levels of psychopathic traits than the control group (Table 2).

TABLE 2 Demographic and Clinical Characteristics of the Sample

	CD Group (n = 28)	Control Group (n = 28)	t Test
Age (mo)	198.38 (17.57)	196.45 (14.27)	0.46
IQ	92.66 (10.15)	103.34 (10.22)	4.00*
Handedness	25 R; 3 L	25 R; 3 L	
ADHD	7.93 (4.45)	0.69 (1.42)	8.34*
symptoms ^a			
Psychopathic traits ^b	122.34 (22.00)	101.31 (15.79)	14.24*

Note: Values in parentheses are standard deviations. ADHD = attention-deficit/hyperactivity disorder; CD = conduct disorder; L = left; R = right.

^aADHD symptoms derived from the ADHD supplement of the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version.

^bPsychopathic traits measured using the total score on the Youth Psychopathic Traits Inventory.

* $p < .05$.

CD and DMN Connectivity

CD was associated with decreased DMN connectivity specifically between the aMPFC and the PCC ($t_{53} = 3.69$, corrected $p = .03$; Figure 1a). Connectivity between other DMN subsystems was unrelated to group status. This decrease in connectivity in the core aMPFC-PCC subsystem remained significant after excluding 16 participants with probable SUDs, although at an uncorrected α level only ($t_{37} = 2.75$, uncorrected $p = .009$; Figure 1b). When the adolescence-onset or childhood-onset CD subgroups were compared with the control group, lower aMPFC to PCC connectivity remained at an uncorrected α level (for adolescence-onset group only: $t_{37} = 2.86$, uncorrected $p = .006$; for childhood-onset group only: $t_{43} = 3.39$, uncorrected $p = .0015$). There were no significant differences in connectivity between the childhood-onset and adolescence-onset CD subgroups, even at an uncorrected level. Interestingly, the CD-related effects were not significant if ADHD symptoms were not included as a covariate, suggesting that important changes in DMN connectivity in patients with CD and comorbid ADHD might be obscured by the fact that CD and ADHD symptoms have opposing effects on DMN connectivity.

To investigate this effect further and study the relative contributions of CD and ADHD to DMN connectivity, the relation between DMN connectivity and ADHD symptoms was tested. Adopting the reverse approach to that described earlier by controlling for group status (i.e., CD versus control group), ADHD symptoms were positively correlated with DMN connectivity (Figure 2). Specifically, functional connectivity between the aMPFC and the PCC ($t_{53} = 3.74$, corrected $p = .03$) and between the aMPFC and the retrosplenial cortex ($t_{53} = 3.48$, corrected $p = .03$) increased as a function of ADHD symptoms. These findings suggest that ADHD is linked to DMN hyperconnectivity, whereas CD is linked to hypoconnectivity in the core DMN subsystem (aMPFC-PCC) only. There were no significant correlations when testing for the effects of the inattentive or hyperactive symptom dimensions of ADHD on DMN connectivity (corrected $p > .10$ for all seed-to-seed correlations).

Psychopathy and DMN Connectivity

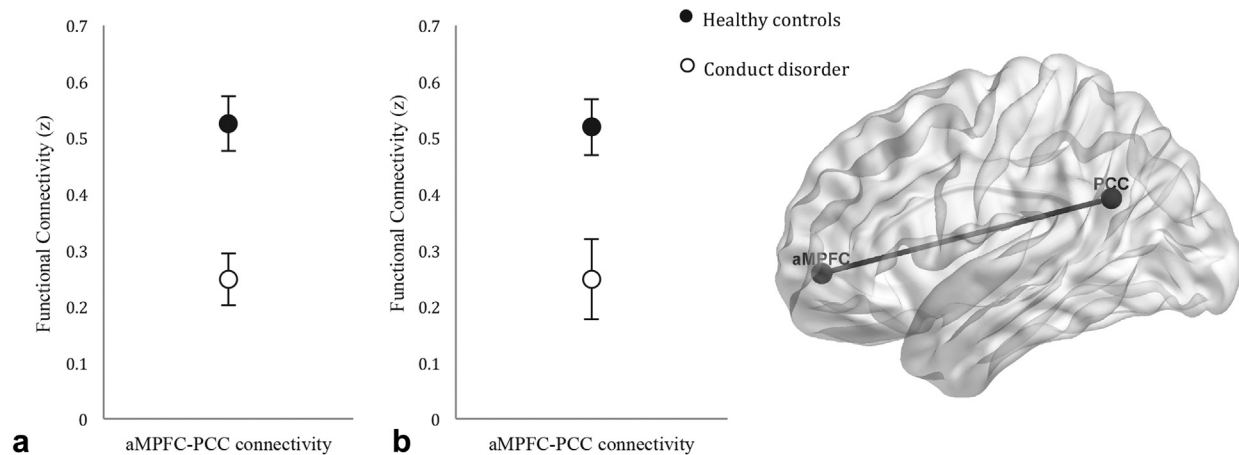
There were no significant associations between total psychopathy scores and DMN connectivity within the CD group. This also was the case for the 3 psychopathy subfactors (i.e., interpersonal, affective, and behavioral); for all seed-to-seed correlations, all corrected p values were greater than .70.

Potential Confounding Factors

Excluding participants with probable SUDs or comorbid ADHD and left-handers did not substantially affect the findings (see Figure 1 and Table S1, available online).

Because the CD and control groups differed in IQ, the authors also tested for correlations with IQ across all participants to examine whether IQ influenced functional

FIGURE 1 Functional connectivity (Fisher z-transformed values) as a function of group status. The results presented in panel a show the data for the entire sample whereas those displayed in panel b are for the subsample without probable substance use disorders. In both cases, the conduct disorder (CD) group showed decreased default mode network connectivity between the anterior medial prefrontal cortex (aMPFC) and posterior cingulate cortex (PCC) compared with healthy controls. Group differences in connectivity are significant at $p < .05$, false discovery rate correction for all seed-to-target pairs or at an uncorrected threshold of $p < .01$. Error bars show standard errors.



connectivity. No significant correlations were found between IQ and DMN connectivity (corrected $p > .40$ for all seed-to-seed correlations).

DISCUSSION

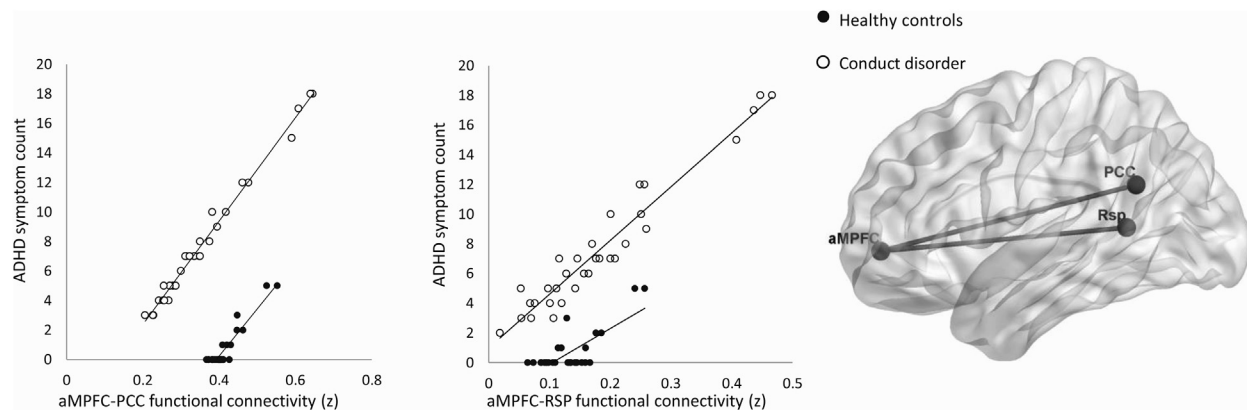
This study tested the hypothesis that CD is associated with decreased connectivity in the DMN, a network previously shown to be important for self-referential and other-referential cognitions. This was done using a seed-based approach to examine connectivity between brain regions known to make up the subsystems of the extended DMN. There were several findings of note.

First, in support of their hypothesis, the authors obtained evidence that CD is linked to significantly decreased aMPFC-PCC connectivity, suggesting impairment in the core hub of the DMN. This effect survived statistical correction for multiple comparisons and was present when controlling for comorbid ADHD symptoms or, at an uncorrected threshold, when excluding participants with probable SUDs or full ADHD diagnoses. Importantly, these effects did not extend to other DMN subsystems and therefore differed from the findings of Dalwani *et al.*,⁶ who found a more generalized DMN deficit in adolescents with CD and comorbid SUDs. The present results are consistent with the recent findings of Zhou *et al.*,²⁵ who also identified DMN hypoconnectivity centered in posterior midline components of the DMN. However, unlike the study by Zhou *et al.*,²⁵ the present study controlled for group differences in IQ and ADHD symptoms, which have been associated with DMN connectivity.^{38,58} This is important given the degree of clinical overlap between ADHD and CD and the robust association between CD and lower IQ.^{59,60}

Second, the authors did not find effects of psychopathic traits or age of onset of CD, 2 factors suggested to delineate between meaningful subtypes of CD, on DMN connectivity. This challenges the view that age of onset can be used to differentiate neurophysiologically distinct subgroups⁴² and extends the literature by demonstrating that DMN abnormalities are observed in childhood-onset and adolescence-onset CD subgroups. The authors also found no effect of psychopathic traits on DMN connectivity. This finding contradicts previous evidence from adult prisoners that reported lower DMN connectivity in individuals with high levels of psychopathic traits compared with typically developing adults. For example, Pujol *et al.*³⁴ compared prisoners with high levels of psychopathic traits with healthy controls, and Motzkin *et al.*³⁵ compared prisoners with high versus low levels of psychopathy. These 2 studies found that connectivity between anterior and posterior midline components of the DMN was decreased in psychopathic individuals compared with control participants. Consistent with these findings, Sethi *et al.*⁶¹ recently compared prisoners with high levels of psychopathy and non-offender controls using diffusion tensor imaging and found decreased fractional anisotropy (measurement of structural connectivity) in the former group in the dorsal cingulum tract that connects midline posterior and anterior DMN components.⁶¹ However, none of these studies controlled for antisocial personality disorder (an adult condition analogous to CD), so the effects reported, which were strikingly similar to those observed in the present study, could have been due to antisocial behavior in general rather than psychopathy per se.

Third, the DMN effects related to CD were present only when controlling for ADHD symptoms. Indeed, ADHD symptoms were associated with increased connectivity

FIGURE 2 Increased functional connectivity (Fisher z-transformed values) as a function of attention-deficit/hyperactivity disorder (ADHD) symptoms. After controlling for group status, participants with high levels of ADHD symptoms show hyperconnectivity between the anterior medial prefrontal cortex (aMPFC) seed and two components of the default mode network: the posterior cingulate cortex (PCC) and the retrosplenial cortex (Rsp). Correlations between ADHD symptoms and connectivity are significant at $p < .05$, false discovery rate correction for all seed-to-target pairs.



within the aMPFC-PCC subsystem when controlling for CD group status. In addition, ADHD symptoms were positively correlated with aMPFC-retrosplenial cortex connectivity. In addition to highlighting the importance of controlling for ADHD symptoms in studies of CD, these findings add to the literature demonstrating ADHD-related alterations in the DMN.⁴¹ The results of previous studies have been inconsistent in this regard. Some have demonstrated DMN hypoconnectivity related to ADHD.^{41,62} The present study, like several others, demonstrated ADHD-related hyperconnectivity.⁵⁷ The reason for this variation among studies is unknown, although it has been suggested these differences reflect the frequent inclusion and failure to control for comorbid disorders (most notably CD).⁶³ The present results suggest that ADHD is associated with intra-DMN hyperconnectivity rather than hypoconnectivity, and that comorbid CD or disruptive behavior disorders might have opposing effects on DMN connectivity.

It should be noted that many other psychiatric disorders have been linked to DMN dysfunction (for a review, see Broyd *et al.*⁵⁹), and therefore abnormalities in this network are not specific to CD. Although the authors showed that their findings of hypoconnectivity in the core aMPFC-PCC subsystem were not the result of co-occurring psychiatric disorders, establishing that this DMN impairment is specific to CD is beyond the scope of the present study because no psychiatric control groups were included. However, the nature of the DMN dysfunction in CD might differ in nature from that observed in other disorders. For example, schizophrenia appears to be associated with decreased DMN connectivity in all subsystems of the network,²⁷ and this has been correlated with subsystem-specific deficits in cognitive processes.²⁸ Likewise, in major depressive disorder,⁶⁴ obsessive-compulsive disorder,⁶⁵ and autistic spectrum disorders,⁶⁶ respectively, there is emerging evidence of disorder-specific abnormalities that

might be tied to individual subcomponents of the DMN. To the authors' knowledge, no empirical study has directly compared DMN connectivity across a range of clinical groups to test the specificity (or otherwise) of DMN disturbances. This would be an interesting avenue for future research.

In terms of the functional significance of DMN hypoconnectivity observed here, the authors hypothesize that this deficit might lead to impairments in self-referential processes that are required for empathy and moral decision making in CD (i.e., judgments about the self and others). Although this prediction has not been tested empirically, it could provide an alternative way of understanding the cognitive features of CD.⁶⁷ For instance, a difficulty in accessing one's own mental states might hinder self-evaluative thinking that could lead to difficulties in learning from punishment⁶⁷ or impair affective empathy.⁶⁸ Beyond social cognition, self-reflection is an important factor in decision making because one frequently has to evaluate a set of possible outcomes before making choices. Several studies have demonstrated that participants with CD have difficulties in adjusting their behavior after negative reinforcement,⁶⁹ show altered sensitivity to gains or losses during choice evaluation,⁷⁰ or discount the value of a reward more sharply with the delay of its receipt.⁷¹ Collectively, these findings have been interpreted as reflecting a present-orientated mindset and a difficulty in prospection⁷²—the ability to build mental representations of future events—which is believed to be mediated by the DMN.

The present study had several strengths, including a relatively large sample, detailed assessment of psychiatric symptoms including CD and ADHD, investigation of the impact of ADHD symptoms on DMN connectivity in CD, and conservative treatment of fMRI artifacts. However, there were some limitations that need to be taken into account.

First, a direct test of the impact of this pattern of altered DMN connectivity on self-referential cognitive processes was beyond the scope of the present study. Nevertheless, there is a wealth of evidence suggesting that synchronization between the PCC and the aMPFC occurs during tasks involving self-referential thought.^{73,74} Second, in accord with Andrews-Hanna *et al.*,¹¹ seeds were placed only in the left hemisphere of the brain. This could have limited the ability to detect group differences in the right hemisphere. Third, analyses of the effects of ADHD symptoms on DMN connectivity would have been strengthened by including individuals with non-comorbid ADHD alone, because the nature of the present sample meant that CD and ADHD symptoms were positively correlated. Fourth, because the analysis was restricted to adolescent boys, the results of this study might not generalize to adolescent girls. Fifth, group differences in IQ could have contributed to the hypo-connectivity findings that were obtained; however, because IQ was included as a covariate of no interest and no significant association was found between IQ and DMN connectivity, this interpretation seems unlikely.

In summary, as predicted, CD was associated with relatively decreased connectivity between anterior and posterior components of the core hub of the DMN. This effect was present only when controlling for comorbid ADHD symptoms. Furthermore, individual differences in psychopathic traits within the CD group were unrelated to DMN connectivity, and childhood- and adolescence-onset CD subgroups appeared to show decreased DMN connectivity compared with typically developing controls. The authors hypothesize that these group differences in DMN connectivity might contribute to the difficulties in empathy and social understanding seen in CD. &

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TABLE S1 Default Mode Network Connectivity Differences Observed When Controlling for Potential Confounding Factors

Contrast	Connectivity	<i>t</i>	<i>P</i> _(uncorrected)
Main effects of CD group status, adjusting for age, IQ, and ADHD symptoms. Sixteen participants with probable SUDs (as assessed using the problem severity scale of the PESQ) excluded.	aMPFC-PCC	2.75	.009
Main effects of CD group status, adjusting for age, IQ, and ADHD symptoms. Seven participants with comorbid ADHD excluded.	aMPFC-LTC	3.01	.004
	aMPFC-PCC	3.57	.0008
Main effects of CD group status, adjusting for age, IQ, and ADHD symptoms. Six left-handed participants excluded.	aMPFC-PCC	3.13	.003
<i>Note:</i> ADHD = attention-deficit/hyperactivity disorder; aMPFC = anterior medial prefrontal cortex; CD = conduct disorder; LTC = lateral temporal cortex; PCC = posterior cingulate cortex; PESQ = Personal Experiences Screening Questionnaire (an indicator of risk for substance use disorders); SUDs = substance use disorders.			